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Comprehension of a simplified assent form in a vaccine trial for adolescents

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Abstract

Introduction—Future HIV vaccine efficacy trials with adolescents will need to ensure that participants comprehend study concepts in order to confer true informed assent. A Hepatitis B vaccine trial with adolescents offers valuable opportunity to test youth understanding of vaccine trial requirements in general.

Methods—Youth reviewed a simplified assent form with study investigators and then completed a comprehension questionnaire. Once enrolled, all youth were tested for HIV and confirmed to be HIV-negative.

Results—123 youth completed the questionnaire (mean age=15 years; 63% male; 70% Hispanic). Overall, only 69 (56%) youth answered all six questions correctly.

Conclusions—Youth enrolled in a Hepatitis B vaccine trial demonstrated variable comprehension of the study design and various methodological concepts, such as treatment group masking.

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INTRODUCTION

It is estimated that in 2010 there were approximately 2.7 million new HIV infections globally with 40% of those new infections occurring in young people, aged 15–24 years.¹ As the vast majority of these infections occur through sexual activity, it is apparent that efforts to promote behavioural modification (eg, through safer sex practices, condom use, etc) are not enough to curtail the persistent rates of HIV within this population. Therefore, other methods, such as a HIV vaccine, may offer the best hope to decrease rates of HIV infection in adolescents and young adults.

To date, many efforts to develop HIV prevention interventions such as microbicides and vaccines have not included adolescents for various reasons. Concerns about adolescent participation in HIV vaccine trials include ethical, legal, behavioural and social implications.²³ Furthermore, past studies which evaluated adolescents' willingness to participate in a HIV vaccine trial demonstrate mixed results.^{4–6} An additional significant concern regarding participation of adolescents in these trials is whether youth are able to comprehend the requirements and stipulations of study participation and therefore, are able to provide true informed assent for research participation.⁷ As defined in the US Code of Federal Regulations for the Protection of Human Subjects in research, *Assent* means a child's affirmative agreement to participate in research.⁸ Mere failure to object should not, absent affirmative agreement, be construed as assent.

Participation in such trials will minimally require adolescents to receive multiple vaccinations and to follow-up with several study visits; to understand study trial concepts; and to agree to participate in HIV prevention education. Therefore, tools that will be necessary for HIV vaccine trials in youth include: a youth-friendly simplified vaccine trial education component with a written test of understanding for participants and guardians; a standardised and effective risk-reduction education programme; and a standardised means for assessment of youth risk behaviours. These tools can be developed, field-tested and finalised in a hepatitis B vaccine trial, which can simulate HIV vaccine trial participation. The present study focused on the first two 'tools' noted above: evaluation of a youth-friendly simplified vaccine trial education component with a written test of understanding for participants prior to enrolment into a randomised Hepatitis B vaccine study conducted by the Adolescent Medicine Trials Network for HIV/AIDS Interventions (ATN).

METHODS

Study site and participants

The primary study, 'Hepatitis B vaccination in youth at ATN sites: Effectiveness of two strategies and evaluation of tools to be used in future HIV prevention trials' (ATN 025; details of the study have been published⁹) was designed to determine immunogenicity of two different hepatitis B vaccines. Briefly, participants were adolescents 12–17 years of age and were recruited from nine ATN sites: Tampa, Florida; Washington, DC; Chicago, Illinois; San Juan, Puerto Rico; Bronx, New York; San Francisco, California; New Orleans, Louisiana; Baltimore, Maryland; and Memphis, Tennessee. Each ATN site provides care to HIV infected youth and participates in HIV risk reduction clinical activities and research studies. For the present study, each site was asked to identify the appropriate venue in their community for recruitment. Each youth assented to study participation and a parent or legal guardian provided written permission.

Procedures

All participants were provided with a simplified assent document specifically developed to enhance comprehension.¹⁰ The assent forms had been reviewed and endorsed by a panel of

ethics experts for the ATN as an example of how to simplify forms without losing content. The assent form presented information at a 6th grade reading level, and used everyday, non-medical language with phrases such as 'shots' instead of 'vaccines'. It was constructed in a question and answer format (eg, 'What am I being asked to do?'), and key concepts were reinforced by supporting graphics. Further, the assent document was reviewed by members of the US Office of Human Research Protection who concurred that the document included the required elements of consent documents outlined in Code of Federal Regulations title 45 part 46.116.⁸

At the screening visit, all youth participants reviewed the simplified assent form with a study investigator, and then completed an Assent Form Comprehension Assessment Questionnaire (six true-false questions; table 1). The assent document and the questionnaire were available in either English or Spanish. Most sites included a study investigator fluent in Spanish; however, sites were permitted to use translators, if requested. Immediately after the youth completed the questionnaire, the study investigator reviewed the results and provided additional teaching on any areas answered incorrectly. Once the investigator and the participant agreed that all important points in the assent were understood, the youth was asked to sign the simplified assent document.

Statistical analysis

Linear models (Statistical Analysis System General Linear Model procedure) were used to evaluate associations between comprehension (total correct scores) and demographic, behavioural risk and other factors.

RESULTS

Mean age (SD) of participants was 15.12 (1.58) years (range: 12–17 years). A majority of the participants were male (62.6%) and identified themselves as Hispanic (69.9%). Most of the Hispanic participants were recruited from one site (Baltimore, Maryland, USA; n=54).

Overall, 69 (56%) youth answered all six questions correctly and 27 (22%) youth answered only five questions correctly. Details regarding the specific questions and responses are shown in table 1.

Twenty-six per cent incorrectly responded that they would be told the identity of the vaccine (Q4). Twenty-one per cent responded that participants in the study would be guaranteed enrolment in future vaccine trials (Q3). Fifteen per cent incorrectly responded they would receive free healthcare through the study (Q5). At least 89% correctly responded to the questions regarding randomisation (Q2) and study withdrawal (Q6).

Finally, among the demographic and behavioural risk factors considered (age, gender, race/ethnicity, weight, sexual identity, sex history, cigarette/alcohol/marijuana use history, site, study retention, study arm), the only factor significantly associated with total correct scores was that participants from the Baltimore, Maryland, USA site (n=67) scored higher than participants from all other sites combined, with average correct scores of 5.45 versus 4.77, respectively, (p=0.0029).

DISCUSSION

Youth enrolled in an ATN Hepatitis B vaccine trial demonstrated variable comprehension of the study and various methodological concepts. Though comprehension overall was high for the majority of participants, additional clarification regarding treatment group masking, possible enrolment in future vaccine trials and lack of provision of free healthcare was needed. Indeed, an additional step of confirming knowledge of important research study

concepts seems necessary to ensure assent, particularly among this adolescent population. Other recent studies have suggested that adults¹¹ and youth¹² may not consistently comprehend important aspects of a clinical trial.

Interestingly, the participants at one site (Baltimore, Maryland, USA) scored significantly better on the questionnaire than those at the other sites. This site enrolled the highest number of Hispanic participants, who had the option of completing the questionnaire in English or Spanish. Though this study did not collect educational background information from the participants, we do not believe that educational differences can account for the discrepancy in questionnaire scores. Instead, we speculate that the study investigators recruiting at this site spent additional time reviewing the assent forms and materials with the participants due to potential language concerns. Indeed, anecdotal evidence from the site personnel indicates that the high number of native Spanish-speaking participants at their site often led to additional rapport building and taking extra time to confirm youths' understanding of the study's objectives and procedures. While not addressed in this study, access to language interpreters for those participants who speak and read English, but whose native language is not English may also be necessary.

Other than this difference by site, there were no factors significantly associated with comprehension. Specifically, age was not related in our data. Younger participants (12–14 years) had slightly higher comprehension than older participants (15–17 years), but this difference was slight and not statistically significant.

Though this trial used a simplified assent form, it is unclear whether Institutional Review Boards will allow assent forms that veer too far in format and language from their own templates. For example, assent forms with pictures and graphics to supplement text may facilitate comprehension for potential participants, but such inclusions in Institutional Review Board-approved assent forms are rare. Instead, some trials employ supplemental material to participants, separate from the assent forms themselves.¹³ Whether supplemental material in vaccine trials facilitates comprehension or adds an additional layer of complexity to a sometimes lengthy assent process needs to be investigated further. Furthermore, this study did not include assessment of comprehension in a comparison group of participants reviewing a non-simplified assent form. Such comparisons of comprehension in future studies would also inform successful enrolment of youth in clinical trials.

Despite the uncertainty regarding the timeline for a HIV vaccine trial that will include adolescents as participants, it is certain that future HIV vaccine and other trials employing biomedical prevention interventions such as microbicides and pre-exposure prophylaxis among adolescents need to maximise comprehension of the essential issues involved in participation in such trials. Whether this is best accomplished by including a simplified assent form, additional follow-up educational components (eg, written questionnaire with feedback), supplemental materials and/or another means will need to be determined. However, the present study suggests that an assessment of understanding via a quiz may be an important step in assuring full comprehension of the study and elements of true informed assent. Full comprehension of vaccine trial concepts by youth is ethical, and will be a crucial element for successful enrolment into vaccine trials in the future, as well as successful participation and retention.

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Table 1

Results from the consent form comprehension assessment questionnaire

Individual question	Frequency (%) of responses	
Q1. Some participants will get a hepatitis B vaccine, and some will get a combined hepatitis A and B vaccine.	True (correct):	114 (92.7%)
	False (incorrect):	9 (7.3%)
Q2. Study nurse decides who gets each vaccine.	True (incorrect):	13 (10.6%)
	False (correct):	110 (89.4%)
Q3. People in the study are guaranteed a chance to be in any future vaccine studies.	True (incorrect):	26 (21.1%)
	False (correct):	97 (78.9%)
Q4. People in the study know which vaccine they are given and when they get the vaccine shot.	True (incorrect):	32 (26.0%)
	False (correct):	91 (74.0%)
Q5. Doctors and nurses give free healthcare to everyone in the study.	True (incorrect):	19 (15.4%)
	False (correct):	104 (84.6%)
Q6. I can withdraw from the study at any time if I choose.	True (correct):	117 (95.1%)
	False (incorrect):	6 (4.9%)